UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,479	02/02/2001	Robert L. Bratzler	C1037/7013 (HCL/MAT)	7139

7590 04/27/2006

Helen C. Lockhart
c/o Wolf Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,479	BRATZLER ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-17 and 38-52* is/are pending in the application.

4a) Of the above claim(s) *41,43,46 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-17,38-40,42,44,45,47,48 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed January 9, 2006 is acknowledged and has been entered. Claims 1-11 and 18-37 have been canceled. Claim 12 has been amended. Claims 12-17, 38-40, 42, 44, 45, 47, 48 and 52 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 41, 43, 46 and 49-51 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 18, 2004.

4. Claims 12-17, 38-40, 42, 44, 45, 47, 48 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are lack positive antecedent basis in the recitation of "allergic asthma"; please see lines 3 and 4 of claim 12.

5. Claims 12-17, 38-40, 42, 44, 45, 47, 48 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no support, description or enablement in the specification for the amendment to the claims reciting "allergic asthmatic event". Applicants have indicated that support for the amendment ("allergic asthmatic event") can be found in the specification at least on page 72 lines 21-22 and in claim 18 as originally filed. However, a review of the section of the specification and originally filed claims does not describe the presently claimed invention. The specification, at page 72, lines 21-22, describes an "asthmatic or allergic event", not an allergic asthmatic event. Originally filed claim 18 does not describe an allergic asthmatic event. Claim 18 depends from claim 12, wherein the immuno-stimulatory nucleic acid is a CpG nucleic acid.

6. Claims 12-17, 38-40, 42, 44, 45, 47, 48 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The pending claims are directed to a method for treating or preventing allergic asthmatic event in a hypo-responsive subject, comprising: administering to a hypo-responsive subject having allergic asthma or at risk of developing allergic asthma an immunostimulatory nucleic acid in an effective amount for

treating or preventing an allergic asthmatic event, wherein the hypo-responsive subject is not a neonate. The claims also recite that sub-therapeutic amounts of an asthma/allergy medicament would be administered to the subject.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed method (see Table 1). The specification teaches that allergic asthma is an allergic condition. The specification discloses a list of commonly used treatment/medicaments for treating asthma/allergy/allergic asthma (see pp. 48-53; Tables 2 and 3). The specification teaches that preventing refers to a prophylactic treatment, which increases the resistance of a subject to an allergen or initiator (p. 58). A sub-therapeutic dosage is a dosage, which is less than that dosage which would produce a therapeutic result in the subject if administered alone; it would not produce the desired therapeutic result in a subject (p. 71). An effective amount of an immunostimulatory nucleic acid and an asthma /allergy medicament refers to the amount necessary or sufficient to realize a desired biologic effect (see pp. 68-69). The specification discloses method steps/procedures, possible dosages and composition components. However, all of these are described in prophetic terms; there is no enablement/examples set forth in the specification of *in vitro* assays, *in vivo* animal models or *in vivo* human examples that would indicate enablement of the claimed invention.

The state of the art is unpredictable with regard to allergic asthma or asthma treatments using immunostimulatory nucleic acids (i.e. CpG). CpG containing . oligonucleotides are currently being investigated for exerting their immuno-therapeutic effects in various organisms. Biological responses to the administration of CpG containing oligonucleotides vary, however, depending on the mode of administration and the organism (see McCluskie et al Molecular Med.,

1999, 5/5:287-300 in its entirety, and especially on p. 296; see Krieg et al, Immunology Today, 2000, 21/10:521-526, especially p. 524). Wohlleben et al 2001 (TRENDS in Immunology, 2001, 22/11:618-626) studied the effects of CpG on atopic disorders such as allergic asthma. CpG-ODNs have multiple stimulatory effects on lymphocytes, including DCs, macrophages, B cells, natural killer (NK) cells and T cells (p. 619). The state of the art questions whether "CpG-ODNs can be used in humans to inhibit the development of asthma? In vitro experiments have shown clearly that human cells react to CpG-DNA in a similar manner to lymphocytes from rodents.... The results obtained from animal models suggest that it is probable that these approaches might also be successful in humans to reduce the development of atopic disorders. However, treatments using CpG-ODNs rely both on innate and adaptive pro-inflammatory Th1 immune responses to inhibit Th2 responses. For this reason, harmful side effects of the treatment need to be ruled out. Besides potential problem of inducing strong inflammatory responses at the site of exposure to allergen, the use of CpG-DNA could also have other serious side effects. It has been reported that the application of CpG-ODNs can cause septic shock in mice. A further potential problem might be the development of autoimmune disease after application of CpG-DNA. Residual autoreactive T cells might become sufficiently activated to cause disease after encountering APCs that have been unspecifically activated by CpG-DNA." (p. 620, col. 2) Wohlleben et al teaches that all approaches that induce Th1 responses have the potential side effects of Th1-cell-mediated inflammation, potentially causing serious tissue damage (p. 624, col. 1). Kline et al 2002 (Am. J. Physiol. Lung Cell Mol. Physiol., 2002, 283:L170-L179; Kline et al, J. Immunol., 1998, 160:2555-2559) teaches that a single treatment of CpG-ODN alone was ineffective in reducing the

manifestations consistent with asthma in this animal model (p. L172, col. 2; see also p. L178, paragraph bridging cols. 1-2). Kline et al 2002 teaches that splenocytes from OVA-treated mice did not develop an antigen-specific Th1 phenotype. However, mice treated with CpG ODN and OVA had a marked shift toward a Th1 response to antigen as well as reduction in airway eosinophilia, serum IgE and bronchial hyperreactivity (p. L176, col. 2).

Weiner (J. Leukocytes Biology, 2000, 68:456-463) states furthermore that the molecular mechanisms of CpG oligonucleotides' immunostimulatory effects are not yet understood (see p. 461). And while the biological effects of some chemical modifications have been studied for CpG containing oligonucleotides, such as 2'-O-methyl modifications, phosphorothioate internucleotide linkages and 5-methyl cytosine substitutions, the incorporation and positioning of chemical modifications relative to the CpG dinucleotide are highly unpredictable (see Agrawal et al Molecular Med. Today, 2000, 6:72-81, especially on pp. 78-80).

Further, Satoh et al (Fukushima Igaku Zasshi, 2002, 52/3:237-250, abstract only) teaches that CpG-ODN is responsible for worsening of allergic contact dermatitis. "S.c. applied CpG ODN one day before sensitization of naïve mice significantly enhanced the ACD to DNFB which showed severe edema with massive CD8+ T cell infiltration." (abstract) Satoh et al also teaches that "[T]hese results indicate that CpG ODN vaccinations may elicit and aggravate side effects such as harmful CD8+ T cell-mediated type IV hypersensitivity responses." (abstract) Dziadzio et al (Handbook of Experimental Pharmacology, 2004, 161(Pharmacology and Therapeutics of Asthma and COPD):273-285, abstract only) teaches that "[V]arious combinations of plasmid DNA, immunostimulatory oligonucleotide (ISS-ODN), and proteins have been studied in murine models to

evaluate the effectiveness of DNA vaccination. The success in skewing the immune response towards a Th1 phenotype in mice still needs to be evaluated in humans. The use of DNA vaccination as a treatment for allergic disease remains a viable option for the future." (abstract) Metzger et al (J. Allergy Clin. Immunol., 1999, 104/2 Pt. 1:260-266) teaches that oligonucleotide therapy for asthma seems unlimited, but confirmation awaits the extension from animal models to human studies (abstract only). The state of the art, taken as a whole, is still unpredictable with regard to the use of ISS-ODN in treating allergic asthma/asthma in an asthmatic subject (human or otherwise) in need of such treatment.

The amount of direction or guidance presented in the specification and the absence of working examples is a hindrance to practicing the claimed invention. Applicants have not provided guidance in the specification toward a method for treating or preventing allergic asthma in a hypo-responsive subject comprising the administration of an immunostimulatory nucleic acid. One skilled in the art would not accept on its face in view of the lack of examples given in the specification as being representative of the successful treatment of asthma or allergic asthma in a hypo-responsive subject comprising the administration of an immunostimulatory nucleic acid (i.e. CpG) in view of the lack of guidance in the specification and the known unpredictability associated with the ability to predict the biological effects exerted by CpG containing oligonucleotides in a hypo-responsive subject. The specification as filed fails to provide particular guidance which resolves the known unpredictability in the art associated with effects provided *in vivo* in a hypo-responsive subject upon administration of CpG containing oligonucleotides, and further whereby treatment effects are provided in a hypo-responsive subject for asthma or allgeric asthma. The quantity of experimentation required to practice the

invention as claimed would require the de novo determination of accessible target sites, modes of delivery and formulations of the CpG to target appropriate cells and/or tissues in a hypo-responsive subject, and further whereby treatment effects are provided for the claimed conditions. Since the specification fails to provide particular guidance for the treatment of allergic asthma comprising administration of CpG containing oligonucleotides and the art teaches that this is not yet possible (i.e. highly unpredictable), it would require undue experimentation to practice the invention as presently claimed.

It is noted that the specification describes the steps of the claimed method to one skilled in the art, but does not provide any evidence that any of the claimed methods would function *in vivo* or *in vitro*. The issue of correlation is related to the issue of the presence or absence of working examples. Correlation as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a working example, if that example correlates with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute working examples. (see MPEP 2164.02) The pending specification does not set forth such correlations for a working example of the claimed *in vivo* method.

Further, the specification would have been enabling as of the filing date involves consideration of the nature of the invention, the state of the prior art and the level of skill in the art. The state of the art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed

invention pertains at the time the application was filed. The specification must be enabling as of the filing date, not evidence provided several years after the date of filing. The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date. (see MPEP 2164.05(a))

In view of all of the above, the pending specification does not enable the claimed invention of a method for treating or preventing allergic asthma in a hypo-responsive subject, comprising: administering to a hypo-responsive subject having allergic asthma or at risk of developing allergic asthma an immunostimulatory nucleic acid in an effective amount for treating or preventing allergic asthma, wherein the hypo-responsive subject is not a neonate.

The rejection is maintained for the reasons of record. Applicant's arguments filed January 9, 2006 have been fully considered but they are not persuasive. Applicant has asserted that the analysis (Wands factors) for determining whether undue experimentation is required and that these factors are to be considered in their totality with no one factor being dispositive of the issue of enablement. While analysis and conclusions of a lack of enablement are based on the Wands factors as required by MPEP 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to use the claimed invention without undue experimentation.

Applicants have asserted that each of the references (Krieg et al 2000, Wohlleben et al 2001, Kline et al 2002, Kline et al 1998, Weiner et al 2000, Satoh et al 2002 and Agrawal et al 2000, Metzger et al 1999) cited to show that the state of the art is unpredictable with regard to the claimed method actually shows promise, may be a promising, probable successful use in humans, potential and/or suggestion of the claimed invention and its enablement. It is noted that even though these references may suggest the possibility of CpG's usefulness, they still also indicate even several years after Applicants' effective filing date that the scope of the use of the claimed composition is not enabled. Further, Weiner cautions that despite therapeutic promise of some CpG ODNs, all CpG ODNs are not alike and more needs to be learned about the heterogenous responses that occur based on host organism, cell subset or CpG ODN sequence. Weiner teaches that the clinical effects of CpG ODN have not yet been explored and further work with the immunostimulatory nucleic acids in both the laboratory and the clinic are needed before their true promise as investigational immunological and therapeutic agents is known.

Applicants have asserted that several Phase I and II studies involving CpG ODN have been performed in humans to date and that these studies demonstrate that CpG ODN are well tolerated in human subjects. Applicants refer to Creticos et al 2002, Simons et al 2004, Krieg et al 2004 as well as others (see pp. 7-8 of Remarks). It is noted that none of the cited references have been provided and they are all post filing. Again, these are results and evidence available after Applicants' effective filing date and it is not clear that these Phase I and II studies were performed in the same manner as set forth in the pending specification.

Applicants have asserted that working examples are not necessary and that the specification provides guidance for the administration immunostimulatory nucleic acids. Applicants have asserted that the skilled practitioner of the art would be aware that one likely route of administration for treatment of allergic asthma in one that delivers a therapeutic composition to airways, e.g. aerosol delivery (see for example, pp. 71-72, 76-79, 25). However, a review of these pages in the specification indicates that these methods and embodiments of the invention are described in prophetic terms. Applicants have asserted that Page 25 lines 22-24 of the specification reads "[m]ost of the asthma/allergy medicaments have been identified. These amounts can be adjusted when they are combined with immuno-stimulatory nucleic acids by routine experimentation." However, a review of page 25 of the pending specification (09/776479) is part of Table 1 (Exemplary immunostimulatory nucleic acids), which covers pp. 12-33.

The amount of direction or guidance presented in the specification and the absence of working examples is a hindrance to practicing the claimed invention. Applicants have not provided guidance in the specification toward a method for treating or preventing an allergic asthmatic event in a hypo-responsive subject comprising the administration of an immunostimulatory nucleic acid to the hypo-responsive subject. One skilled in the art would not accept on its face in view of the lack of any working examples in the specification as being representative of the successful treatment or prevention of an allergic asthmatic event in a hypo-responsive subject comprising the administration of an immunostimulatory nucleic acid (i.e. CpG) in view of the lack of guidance in the specification and the known unpredictability associated with the ability to predict the biological effects exerted by CpG containing oligonucleotides in a subject. The specification as filed fails to

provide particular guidance which resolves the known unpredictability in the art associated with effects provided *in vivo* in a subject upon multiple administrations of CpG containing oligonucleotides, and further whereby treatment effects are provided in a hypo-responsive subject for allergic asthmatic events. The quantity of experimentation required to practice the invention as claimed would require the de novo determination of accessible target sites, modes of delivery and formulations of the CpG to target appropriate cells and/or tissues in a subject, and further whereby treatment effects are provided for the claimed conditions. Since the specification fails to provide particular guidance for the treatment or prevention of an allergic asthmatic event in a hypo-responsive subject comprising administration of CpG containing oligonucleotides and the art teaches that this is not yet possible (i.e. highly unpredictable), it would require undue experimentation to practice the invention as presently claimed.

It is noted that the specification describes the steps of the claimed method to one skilled in the art, but does not provide any evidence that any of the claimed methods would function *in vivo* or *in vitro*. The issue of correlation is related to the issue of the presence or absence of working examples. Correlation as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a working example, if that example correlates with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute working examples. (see MPEP 2164.02) The pending specification does not set forth such correlations for a working example of the claimed *in vivo* method.

The claimed invention must be enabled as of the filing date of the patent application, not enabled by publications post filing. Whether the specification would have been enabling as of the filing date involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art. The initial inquiry is into the nature of the invention, i.e., the subject matter to which the claimed invention pertains. The nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art.

The state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains at the time the application was filed. See MPEP § 2164.05(b).

The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification.

The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date. 35 U.S.C. 112 requires the specification to be enabling only to a person "skilled in the art to which it pertains, or with which it is most nearly connected." In general, the pertinent art should be defined in terms of

the problem to be solved rather than in terms of the technology area, industry, trade, etc. for which the invention is used.

The specification need not disclose what is well known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application").< Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976) (In general, if an applicant seeks to use a patent to prove the state of the art for the purpose of the enablement requirement, the patent must have an issue date earlier than the effective filing date of the application.). While a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). In general, the examiner should not use post-filing date

references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application. In re Hogan, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977). If individuals of skill in the art state that a particular invention is not possible years after the filing date that would be evidence that the disclosed invention was not possible at the time of filing and should be considered. In In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513-14 (Fed. Cir. 1993) an article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms. Claims not directed to the specific virus and the specific animal were held nonenabled.

Further, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). Although, typically, inoperative embodiments are excluded by language in a claim (e.g., preamble), the scope of the claim may still not be enabled where undue experimentation is involved in determining those embodiments that are operable. A disclosure of a large number of operable embodiments and the identification of a single

inoperative embodiment did not render a claim broader than the enabled scope because undue experimentation was not involved in determining those embodiments that were operable. In re Angstadt, 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976). However, claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). The scope of the pending claims administers any immunostimulatory nucleic acid to a hypo-responsive subject to treat or prevent an allergic asthmatic event.

Applicants have asserted that McCluskie et al is an article describing DNA vaccines against Hepatitis B virus. On page 296, the page identified by the examiner, the reference mentions that one of the factors involved in influencing the Th bias of the response to DNA vaccines is the presence of CpG motifs. The reference is not relevant to the enablement of the pending claims because the pending claims do not encompass plasmid vectors (or DNA vaccines). The pending independent claims are directed to the use of oligonucleotides. The issues of predictability and therapeutic effectivity are very different for CpG oligo-nucleotides and DNA vaccines. However, the claims do not recite that any kind of protein or antigen was added in the composition of the CpG immunostimulatory nucleic acid being administered; the claims do not specifically exclude plasmids, vectors or DNA vaccines. The immunostimulatory nucleic acid could read on the whole bacteria, or the immunostimulatory nucleic acid could be part of a DNA vaccine; the claims just recite a CpG immunostimulatory nucleic acid.

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
April 24, 2006